In the Specification:

Please amend the specification as shown:

Please delete the original Sequence Listing.

Page 21, after the last line, beginning on a new page, please insert the attached substitute Sequence Listing.

Please delete the paragraph on page 3, lines 21-37 and replace it with the following paragraph:

Therefore, the present invention provides the use of a compound comprising the following amino acid sequence

$$X_1X_2X_3X_4X_5X_6,$$

wherein X_1 is an amino acid, except of C,

X_2 is an amino acid, except of C,

X_3 is an amino acid, except of C,

X_4 is an amino acid, except of C,

X_5 is an amino acid, except of C,

X_6 is an amino acid, except of C,

and wherein $X_1X_2X_3X_4X_5X_6$ is not DAEFRH **(SEQ ID NO: 1)**, said compound having a binding capacity to an antibody being specific for the natural N-terminal Aβ42 sequence DAEFRH **(SEQ ID NO: 1)**, and 5-mers thereof having a binding capacity to said antibody being specific for the natural N-terminal Aβ42 sequence DAEFRH **(SEQ ID NO: 1)**, for the preparation of a vaccine for Alzheimer's disease (AD).

Please delete the paragraphs on page 5, lines 1-37 and replace them with the following paragraphs:

The antibody used for the mimotope identification according to the present invention detects the Aβ-derived amino acid sequence DAEFRH **(SEQ ID NO: 1)** (= original epitope) with a free amino terminal aspartic acid, thus it does not recognize native APP. The antibody may be a monoclonal or polyclonal antibody preparation or any antibody part or derivative thereof, the only prerequisite is that the antibody molecule specifically recognises the DAEFRH **(SEQ ID NO: 1)** epitope, i.e. that it does not bind to the natural N-terminally prolonged forms of the amyloid precursor protein, which means that the binding capacity to the DAEFRH **(SEQ ID NO: 1)** epitope is at least 100 times, preferably at least 1000 times, more preferred at least 10^5 times, higher than to the APP molecule. The antibody may be an antibody showing the same or a higher binding capacity to the DAEFRH **(SEQ ID NO: 1)** sequence as the antibody described by Johnson-Wood et al., 1997. Of course, also antibodies with a lower binding capacity may be used (>10 %, >50 % or >80 % of the binding capacity of the Johnson-Wood et al. antibody), although the higher binding capacity is more preferred.

The compounds according to the present invention bind to those antibodies with comparable specificity as the DAEFRH **(SEQ ID NO: 1)** sequence.

Preferably, the compound to be used according to the present invention comprises or is consisting of a peptide, wherein
X_1 is G or an amino acid with a hydroxy group or a negatively charged amino acid, preferably E, Y, S or D,
X_2 is a hydrophobic amino acid or a positively charged amino acid, preferably I, L, V, K, W, R, Y, F or A,
X_3 is a negatively charged amino acid, preferably D or E,
X_4 is an aromatic amino acid or L, preferably Y, F or L,
X_5 is H, K, Y, F or R, preferably H, F or R, and
X_6 is S, T, N, Q, D, E, R, I, K, Y, or G, preferably T, N, D, R, I or G,
especially EIDYHR **(SEQ ID NO: 91)**, ELDYHR **(SEQ ID NO: 92)**, EVDYHR **(SEQ ID NO: 93)**, DIDYHR **(SEQ ID NO: 94)**, DLDYHR **(SEQ ID NO: 95)**, DVDYHR **(SEQ ID NO: 96)**, DIDYRR **(SEQ ID NO: 97)**, DLDYRR **(SEQ ID NO: 98)**, DVDYRR **(SEQ ID NO: 99)**,

DKELRI **(SEQ ID NO: 100)**, DWELRI **(SEQ ID NO: 101)**, YREFRI **(SEQ ID NO: 102)**, YAEFRG **(SEQ ID NO: 103)**, EAEFRG **(SEQ ID NO: 104)**, DYEFRG **(SEQ ID NO: 105)**, ELEFRG **(SEQ ID NO: 106)**, DRELRI **(SEQ ID NO: 107)**, DKELKI **(SEQ ID NO: 108)**, DRELKI **(SEQ ID NO: 109)**, GREFRN **(SEQ ID NO: 110)**, EYEFRG **(SEQ ID NO: 111)**, DWEFRDA **(SEQ ID NO: 112)**, SWEFRT **(SEQ ID NO: 113)**, DKELR **(SEQ ID NO: 114)** or SFEFRG **(SEQ ID NO: 115)**.

Please delete the paragraphs on page 6, line 36 to page 7, line 32 and replace them with the following paragraphs:

According to another aspect, the present invention further relates to a method for isolating a compound binding to an antibody being specific for the natural N-terminal Aβ42 sequence DAEFRH **(SEQ ID NO: 1)** comprising the steps of

- providing a peptide compound library comprising peptides containing the following amino acid sequence

$$X_1X_2X_3X_4X_5X_6,$$

wherein X_1 is an amino acid, except of C,
X_2 is an amino acid, except of C,
X_3 is an amino acid, except of C,
X_4 is an amino acid, except of C,
X_5 is an amino acid, except of C,
X_6 is an amino acid, except of C,
and wherein $X_1X_2X_3X_4X_5X_6$ is not DAEFRH **(SEQ ID NO: 1)**,

- contacting said peptide library with said antibody and
- isolating those members of the peptide library which bind to said antibody.

According to a specific embodiment of this aspect, the present invention relates to a method for isolating a compound binding to an antibody being specific for the natural N-terminal Aβ42 sequence DAEFRH **(SEQ ID NO: 1)** comprising the steps of

- providing a peptide compound library comprising peptides containing the following amino acid sequence

$$X_1X_2X_3X_4X_5X_6,$$

wherein X_1 is a natural amino acid, except of K and C,
X_2 is a natural amino acid, except of C,
X_3 is a natural amino acid, except of K and C,

X_4 is a natural amino acid, except of K and C,
X_5 is a natural amino acid, except of C,
X_6 is a natural amino acid, except of P and C, and wherein $X_1X_2X_3X_4X_5X_6$ is not DAEFRH **(SEQ ID NO: 1)**,

- contacting said peptide library with said antibody and
- isolating those members of the peptide library which bind to said antibody.

Please delete the paragraph on page 8, lines 27-29 and replace it with the following paragraph:

The library has to be constructed to exclude the naturally occurring Aβ sequence (e.g. DAEFRH **(SEQ ID NO: 1)**), since vaccination with this sequence is clearly excluded from this invention.

Please delete the paragraph on page 8, line 35 to page 9, line 15 and replace it with the following paragraph:

The present invention also relates to a composition comprising an anti N-terminal Aβ42-antibody-binding peptide (or, in certain cases preferred, a larger molecule comprising such a peptide (e.g. the peptide linked to a carrier or delivery molecule)) as defined herein (optionally as single effective component), preferably to a vaccine against Alzheimer's Disease comprising such an antigen, especially an antigen which includes at least one peptide selected from the group EIDYHR **(SEQ ID NO: 91)**, ELDYHR **(SEQ ID NO: 92)**, EVDYHR **(SEQ ID NO: 93)**, DIDYHR **(SEQ ID NO: 94)**, DLDYHR **(SEQ ID NO: 95)**, DIDYHR **(SEQ ID NO: 96)**, DIDYRR **(SEQ ID NO: 97)**, DLDYHR **(SEQ ID NO: 98)**, DVDYRR **(SEQ ID NO: 99)**, DKELRI **(SEQ ID NO: 100)**, DWELRI **(SEQ ID NO: 101)**, YREFRI **(SEQ ID NO: 102)**, YAEFRG **(SEQ ID NO: 103)**, EAEFRG **(SEQ ID NO: 104)**, DYEFRG **(SEQ ID NO: 105)**, ELEFRG **(SEQ ID NO: 106)**, DRELRI **(SEQ ID NO: 107)**, DKELKI **(SEQ ID NO: 108)**, DRELKI **(SEQ ID NO: 109)**, GREFRN **(SEQ ID NO: 110)**, EYEFRG **(SEQ ID NO: 111)**, DWEFRDA **(SEQ ID NO: 112)**, SWEFRT **(SEQ ID NO: 113)**, DKELR **(SEQ ID NO: 114)**or SFEFRG **(SEQ ID NO: 115)**. These peptides are - besides the other peptides provided with the present invention specifically suited to be used for the preparation of a pharmaceutical composition, especially for AD vaccines. These sequences are purely artificial Aβ-mimotopes. The peptides may - for vaccination purposes - be coupled (covalently or non-covalently) to suitable carriers and may be provided as peptide

compounds or complexes together with other compounds or moieties, e.g. adjuvants, peptide or protein carriers, etc. and administered in a suitable manner (as e.g. described in O'Hagan et al., Nature Reviews, Drug Discovery 2(9)(2003), 727-735).

Please delete the paragraphs on page 9, lines 20-26 and replace them with the following paragraphs:

Fig. 1 shows the individualised peptide members of library 4 used for the present screening process **(SEQ ID NOS 1 and 1-90, respectively, in order of appearance)**.

Fig. 2 shows an inhibition assay with mimotopes for DAEFRH **(SEQ ID NO: 1)**.

Fig. 3 shows another inhibition assay with other mimotopes for DAEFRH **(SEQ ID NO: 1)**.

Please delete the paragraph on page 9, line 38 to page 10, line 9 and replace it with the following paragraph:

Mice are vaccinated with the 6mer peptide DAEFRH **(SEQ ID NO: 1)** (natural N-terminal Aβ42 sequence) linked to the protein bovine serum albumin BSA (to make use of the hapten-carrier-effect), emulsified in CFA (first injection) and IFA (booster injections). DAEFRH-peptide-specific **(DAEFRH sequence disclosed as SEQ ID NO: 1)**, antibody-producing hybridomas are detected by ELISA (DAEFRH-peptide-coated ELISA plates **(DAEFRH sequence disclosed as SEQ ID NO: 1)**). Peptide SEVKMDAEFRH **(SEQ ID NO: 116)** (natural N-terminally prolonged sequence, APP-derived, containing the Aβ42-derived sequence DAEFRH **(SEQ ID NO: 1)**) is used as negative control peptide: hybridomas recognizing the prolonged peptide are excluded because they do not distinguish between Aβ42-derived peptides with free aspartic acid at the N-terminus and APP-derived peptide DAEFRH **(SEQ ID NO: 1)** without free aspartic acid.

Please delete the paragraph on page 12, lines 11-17 and replace it with the following paragraph:

For the present examples, the antibody described in example 1 is used for screening peptide libraries, however, any antibody preparation specifically recognizing the DAEFRH-sequence **(SEQ ID NO: 1)**, but not the naturally N-terminally prolonged sequence of the Aβ molecule (e.g. MDAEFRH **(SEQ ID NO: 117)**, KMDAEFRH **(SEQ ID NO: 118)**, SEVKMDAEFRH **(SEQ ID NO: 116)**or the complete amyloid (precursor) protein, APP), such as e.g. described by Johnson-Wood et al., 1997.

Please delete the paragraph on page 14, lines 15-17 and replace it with the following paragraph:

The 6mer peptides EIDYHR **(SEQ ID NO: 91)**, ELDYHR **(SEQ ID NO: 92)**, and EVDYHR **(SEQ ID NO: 93)** are examples for mimotopes that can be detected by the monoclonal antibody produced according to example 1. above.

Please delete the paragraph on page 14, lines 37-39 and replace it with the following paragraph:

The 6mer peptides DIDYHR **(SEQ ID NO: 94)**, DLDYHR **(SEQ ID NO: 95)**, and DVDYHR **(SEQ ID NO: 96)** are examples for mimotopes that can be detected by the monoclonal antibody produced according to 1. above.

Please delete the paragraphs on page 15, lines 20-28 and replace them with the following paragraphs:

The 6mer peptides DLDYRR **(SEQ ID NO: 97)**, DLDYRR **(SEQ ID NO: 98)**, and DVDYRR **(SEQ ID NO: 99)** are examples for mimotopes that can be detected by the monoclonal antibody produced according to 1. above (D in position 1 and R in position 5 are identical with the original epitope).

2.4.: Library 4: This peptide library 4 consists of 5 x 18 = 90 peptides, is commercially available from Mimotopes Ltd. (Paris, France; see manufacturer's guidelines) and is designed according to the natural N-terminal Aβ42 sequence DAEFRH **(SEQ ID NO: 1)**.

Please delete the paragraph on page 16, lines 1-5 and replace it with the following paragraph:

The individualised peptide members of library 4 are depicted in fig. 1. Peptides no. 1, 24, 48, 56 and 80 have the original sequence of the Aβ42 N-terminal sequence. All other peptides are candidate peptides which are tested with respect to their binding capacity to a DAEFRH-binding antibody**(DAEFRH sequence disclosed as SEQ ID NO: 1)**.

Please delete the paragraph on page 16, lines 21-37 and replace it with the following paragraph:

The peptide library is dissolved in 100% DMS0 (final concentration 10 mg/ml).

The peptide solution is further diluted in PBS.

The peptide mixture is coated overnight (4 °C) onto ELISA plates (Nunc Maxisorp, Germany), starting with 500 μg/well, and titrated to 100 ng/well.

The plates are washed 3x times with PBS/Tween 20 (0.1% v/v).

The plates are blocked with PBS/BSA (2 h at room temperature).

The plates are washed 3x times with PBS/Tween.

The plates are incubated with biotinylated DAEFRH-specific mAb **(DAEFRH sequence disclosed as SEQ ID NO: 1)** (10 μg/m1 in PBS) for 4 h at room temperature.

The plates are washed 3x times with PBS/Tween.

The plates are incubated with streptavidin-horseradish-peroxidase (30 min at room temperature).

The plates are washed 5x times with PBS/Tween.

The plates are incubated with ABTS + H2O2 (0.1 % w/v; 10 to 45 min) and the reaction is stopped with citric acid followed by photometric evaluation (wavelength 405 nm).

Please delete the paragraphs on page 18, line 4 to page 19, line 13 and replace them with the following paragraphs:

The following peptides are used:

Peptide 1737 DAEFRH **(SEQ ID NO: 1)**

Peptide 3001 DKELRI **(SEQ ID NO: 100)**

Peptide 3002 DWELRI **(SEQ ID NO: 101)**

Peptide 3003 YREFFI **(SEQ ID NO: 119)**

Peptide 3004 YREFRI **(SEQ ID NO: 102)**

Peptide 3005 YAEFRG **(SEQ ID NO: 103)**

Peptide 3006 EAEFRG **(SEQ ID NO: 104)**

Peptide 3007 DYEFRG **(SEQ ID NO: 105)**

Peptide 3008 ELEFRG **(SEQ ID NO: 106)**

Peptide 3009 SFEFRG **(SEQ ID NO: 115)**

Peptide 3010 DISFRG **(SEQ ID NO: 120)**

Peptide 3011 DIGWRG **(SEQ ID NO: 121)**

Procedure:

ELISA plates (Nunc Maxisorp) are coated with the original peptide epitope DAEFRH **(SEQ ID NO: 1)** (C-terminally prolonged with C and coupled to bovine serum albumin BSA) at a

concentration of 0.1 μg/m1 peptide-BSA (100μl/well, 12h, 4°C). After blocking with PBS/BSA 1% (200μl/well, 12h, 4°C), the plates are washed 3x times with PBS/Tween. Then, biotinylated monoclonal antibody (1:2000, 50μl/well) and peptides (50μl/well) at 50, 5, 0.5, 0.05, 0.005, and 0.0005 μg/ml are added for 20 min. at 37°C. The plates are washed 3x times with PBS/Tween and are incubated with horseradish peroxidase (HRP)-labeled streptavidin (100μl/well, 30 min, RT). The plates are washed 5x times with PBS/Tween and are incubated with ABTS + H2O2 (0.1% w/v, 10 to 45 min) and the reaction is stopped with citric acid followed by photometric evaluation (wavelength 405 nm).

As expected and seen in Fig. 2, peptide 1737 DAEFRH **(SEQ ID NO: 1)** can compete with BSA-coupled, plate-bound peptide DAEFRH **(SEQ ID NO: 1)** and thus inhibits recognition by the monoclonal antibody. Furthermore, it is shown that peptide 3003 is not able to inhibit binding of the monoclonal antibody to the original epitope. In contrast, peptides 3001, 3002, 3004, 3005, 3006, and 3007 (to a different extent) block epitope recognition. Whereas peptide 3004 is only inhibitory at a high concentration (50 μg/ml), peptides 3001, 3006, and 3007 are strongly inhibitory with an IC50 of less than 0.5 μg/ml. Peptides 3002 and 3005 are "intermediate" inhibitors with an IC50 of more than 0.5 μg/ml.

As expected and seen in Fig. 3, peptide 1737 DAEFRH **(SEQ ID NO: 1)** can successfully compete with BSA-coupled, plate-bound peptide DAEFRH **(SEQ ID NO: 1)** for monoclonal antibody recognition in an additionally performed, independent experiment. Furthermore, it is shown that peptides 3010 and 3011 are not inhibitory at the concentrations tested, whereas peptides 3008 and 3009 are (relatively) weak inhibitors with an IC50 of less than 5 μg/ml.

Please delete Table 1 and replace it with the following table:

Table 1: Inhibitory capacity of mimotopes:

Peptide 3001 DWELRI **(SEQ ID NO: 100)**	strong
Peptide 3002 DWELRI **(SEQ ID NO: 101)**	intermediate
Peptide 3003 YREFFI **(SEQ ID NO: 119)**	none

Peptide 3004 YREFRI **(SEQ ID NO: 102)** weak

Peptide 3005 YAEFRG **(SEQ ID NO: 103)** intermediate

Peptide 3006 EAEFRG **(SEQ ID NO: 104)** strong

Peptide 3007 DYEFRG **(SEQ ID NO: 105)** strong

Peptide 3008 ELEFRG **(SEQ ID NO: 106)** weak

Peptide 3009 SFEFRG **(SEQ ID NO: 115)** weak

Peptide 3010 DISFRG **(SEQ ID NO: 120)** none

Peptide 3011 DIGWRG **(SEQ ID NO: 121)** none

Please delete the paragraphs on page 20, line 6 to page 21, line 17 and replace them with the following paragraphs:

The following peptides are used:

Peptide 1737 DAEFRH **(SEQ ID NO: 1)** (original epitope + C)

Peptide 1234 KKELRI **(SEQ ID NO: 122)**

Peptide 1235 DRELRI **(SEQ ID NO: 107)**

Peptide 1236 DKELKI **(SEQ ID NO: 108)**

Peptide 1237 DRELKI **(SEQ ID NO: 109)**

Peptide 1238 DKELR **(SEQ ID NO: 114)**

Peptide 1239 EYEFRG **(SEQ ID NO: 111)**

Peptide 1241 DWEFRDA **(SEQ ID NO: 112)**

Peptide 4002 SWEFRT **(SEQ ID NO: 113)**

Peptide 4003 GREFRN **(SEQ ID NO: 110)**

Peptide 4004 WHWSWR **(SEQ ID NO: 123)**

Procedure:

ELISA plates (Nunc Maxisorp) are coated with the original peptide epitope DAEFRH **(SEQ ID NO: 1)** (C-terminally prolonged with C and coupled to bovine serum albumin BSA) at a concentration of 0.1 μg/ml peptide-BSA (100μl/well, 12h, 4°C). After blocking with PBS/BSA 1% (200μl/well, 12h, 4°C), the plates are washed 3x times with PBS/Tween. Then, biotinylated monoclonal antibody (1:2000, 50μl/well) and peptides (50μl/well) at different concentrations are added for 20 min. at 37°C. The plates are washed 3x times with PBS/Tween and are incubated with horseradish peroxidase (HRP)-labeled streptavidin (100μl/well, 30 min, RT). The plates are washed 5x times with PBS/Tween and are incubated with ABTS H2O2 (0.1% w/v, 10 to 45 min) and the reaction is stopped with citric acid followed by photometric evaluation (wavelength 405 nm).

As expected and seen in Fig. 4, peptide 1737 DAEFRH **(SEQ ID NO: 1)** can compete with BSA-coupled, plate-bound peptide DAEFRH **(SEQ ID NO: 1)** and thus inhibits recognition by the monoclonal antibody. Furthermore, it is shown that peptide 4004 is not able to inhibit binding of the monoclonal antibody to the original epitope. In contrast, peptides 4002 and 4003 (to a different extent) block epitope recognition. Whereas peptide 4003 is only inhibitory at a relatively high concentration (10 μg/ml), peptide 4002 is strongly inhibitory with an IC50 of less than 0.4 μg/ml.

As expected and seen in Fig. 5, peptide 1737 DAEFRH **(SEQ ID NO: 1)** can successfully compete with BSA-coupled, plate-bound peptide DAEFRH **(SEQ ID NO: 1)** for monoclonal antibody recognition in an additionally performed, independent experiment. Furthermore, it is shown that peptide 1234 is hardly inhibitory at the concentrations tested, whereas peptides 1235, 1236, 1237, 1238, 1239 and 1241 (to a different extent) block epitope recognition. Peptides 1235, 1238 and 1241 are strong inhibitors with an IC50 of less than 0.5 μg/ml, whereas peptides 1236 and 1237 are (relatively) weak inhibitors with an IC50 of more than 5 μg/ml. Peptide 1239 is an intermediate inhibitor with an IC50 of more than 0.5 μg/ml.

Please delete Table 2 and replace it with the following table:

Table 2: Inhibitory capacity of mimotopes:

Peptide 1234 KKELRI **(SEQ ID NO: 122)**	none
Peptide 1235 DRELRI **(SEQ ID NO: 107)**	strong
Peptide 1236 DKELKI **(SEQ ID NO: 108)**	weak
Peptide 1237 DRELKI **(SEQ ID NO: 109)**	weak
Peptide 1238 DKELR **(SEQ ID NO: 114)**	strong
Peptide 1239 EYEFRG **(SEQ ID NO: 111)**	intermediate
Peptide 1241 DWEFRDA **(SEQ ID NO: 112)**	strong
Peptide 4002 SWEFRT **(SEQ ID NO: 113)**	strong
Peptide 4003 GREFRN **(SEQ ID NO: 110)**	weak
Peptide 4004 WHWSWR **(SEQ ID NO: 123)**	none

Please delete the paragraph on page 21, lines 35-39 and replace it with the following paragraph:

The results presented in Figures 4 and 5 show that in addition to various 6mer peptides (as shown here and before), 5mer peptides (namely peptide 1238 DKELR **(SEQ ID NO: 114)**) and 7mer peptides (namely peptide 1241 DWEFRDA **(SEQ ID NO: 112)**) may be used as epitopes in a mimotope-based Alzheimer vaccine.